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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,544	02/14/2005	Michael W. Dahm	24741-1538	1428

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EXAMINER	
GUSSOW, ANNE	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,544	DAHM, MICHAEL W.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *8-10 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *February 14, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 1-7, 11, and 12, in the reply filed on January 11, 2007 is acknowledged.

2. Claims 8-10 and 13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on January 11, 2007.

3. Claims 1-7, 11 and 12 are under examination.

Information Disclosure Statement

4. The information disclosure statement filed February 14, 2005 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it contains foreign references without English translations. The documents WO 2000/46585 and Alexander Goetz, Bioforum 2001 have not been considered and are crossed through on the IDS which is included in the mailing of this action. Applicant is requested to submit an English translation of the documents for them to be considered in prosecution of this application. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining

compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Specification

5. The disclosure is objected to because of the following informalities: the specification contains typographical errors. For example, on page 29 line 17 "bond marrow" should be "bone marrow"

Appropriate correction is required throughout.

6. The use of the trademarks Ficoll®, Oncoquick®, Leucosep®, and LightCycler™ have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The trademark symbols are missing for LightCycler™ on page 18, Oncoquick® on page 30, and Ficoll® on page 29.

Appropriate correction is required for all trademarks throughout.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-7, 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting disseminated tumor cells from body fluids by density gradient separation in a vessel divided by a porous barrier, a filter, a sieve or a flap, wherein the enriched cells express cytokeratins 8, 18, 19, and 20 does not reasonably provide enablement for detecting disseminated tumor cells, wherein the enriched cells express cytokeratins 1-7, and 9-17. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

> Wands states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to a method for detecting disseminated tumor cells from any body fluid by density gradient separation in a vessel divided by a porous

barrier, a filter, a sieve, or a flap, wherein the enriched cells express at least one epithelial marker from cytokeratins 1-20.

The specification discloses a method for detecting disseminated tumor cells from peripheral blood (page 19 line 5) by density gradient separation in an Oncoquick separation vessel, which is divided by a porous barrier (page 17 line 8), and detection of cytokeratins 8, 18, 19, and 20 in the enriched cell population (page 26 lines 7-15 and page 21 lines 35-37). Applicants have not provided any direction or guidance to assist one skilled in the art in the detection of disseminated tumor by detecting other cytokeratins (1-7 or 9-17).

Cytokeratins have been detected in both normal and cancerous cells. Traweek, et al. (American Journal of Pathology, 1993, Vol. 142 No. 4, pages 1111-118) teach the detection of cytokeratins 8 and 18 in normal endothelial cells, lymph node, and peripheral blood mononuclear cells in addition to the cancerous myeloid leukemia cell line HL-60, non-Hodgkin's lymphoma, and leiomyosarcoma (table 1 and page 1113 1st column). Traweek, et al. also teach variability in the detection of cytokeratin 19 in leiomyosarcoma and non-Hodgkin's lymphoma samples (page 1114 2nd column). Cytokeratin 19 is the most commonly used marker to detect minimal residual disease (micro metastasis) in breast cancer, although in other solid tumors cytokeratin is insufficiently sensitive and/or specific for detection (Slade and Coombes, Nature Clinical Practice Oncology, 2007, Vol. 4 No. 1, pages 30-41, see page 36 1st column).

Additionally, Slade and Coombes teach that one problem with analyses of minimal residual disease is that not all patients with positive bone marrow results

relapse and those with negative bone marrow results might relapse (page 32 2nd column). Thus, Traweek, et al. and Slade and Coombes suggest that cytokeratins 8, 18, and 19 are not independently reliable markers for the detection of disseminated cancer cells.

In view of the lack of predictability of the art to which the invention pertains and the lack of established protocols for detecting disseminated cancer cells by detecting cytokeratins, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for detecting disseminated cancer cells in body fluid by detecting cytokeratins 1-20, commensurate in scope with the claimed invention.

Conclusion

9. No claims are allowed.

10. Claims 1-7, 11, and 12 are free of the prior art. The closest prior art is Dahm, et al. (U.S. Pat 6,821,726, PCT filed August 12, 1999).

Dahm, et al. teach a method for quantitatively analyzing tumor cells in a body fluid comprising enrichment of tumor cells by covering a suspension medium of a density in the range from 1.055 to <1.070 g/mL with a layer of body fluid (column 9 lines 40-44) in a vessel which is divided into an upper and lower compartment by a porous

barrier, a filter or sieve having a thickness of 1-10 mm (column 11 lines 36-51) and a pore size of 20-100 μm (column 11 lines 63-65) wherein the porous barrier is made of a hydrophobic material or is coated with a hydrophobic material (column 12 lines 4-6) and a dye is added to the cell separation medium to render the interphase between the cell separation medium and body fluid more visible (column 12 lines 37-44). Dahm, et al. teach detecting expression of telomerase in the enriched population of cells (column 20, lines 33-67). Dahm, et al. do not teach or reasonably suggest determination of whether the enriched cells express any epithelial markers including the cytokeratins 1-20.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

February 21, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER